AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

1. (Currently amended) A compound of formula I:

or a pharmaceutically acceptable salt or mixtures thereof,

wherein R¹ is selected from -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹; L is an optionally substituted C₁₋₆ alkylidene chain wherein up to two non-adjacent methylene units of L are optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NRCO₂, CO, CO₂, CONR, CSNR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O); m is 0 or 1; Ar¹ is an optionally substituted aryl group selected from a 3-8 membered monocyclic or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and Cy¹ is an optionally substituted group selected from a 3-7-membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10-membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein Ar¹ and Cy¹ are each independently optionally substituted with y occurrences of Z-R^Y; wherein Z is a bond or is a C₁-C₆ alkylidene chain wherein up to two non-adjacent methylene units of Z are optionally replaced by CO, CO₂, COCO, CONR, CSNR, OCONR, NRNR, NRNRCO, NRCO, NRCS, NRCO₂, NRCONR, NRCSNR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; each occurrence of R^Y is independently selected from R', halogen, NO₂, CN, OR', SR', N(R')₂, NR'C(O)R', NR'C(S)R', $NR'C(O)N(R')_2$, $NR'C(S)N(R')_2$, $NR'CO_2R'$, C(O)R', CO_2R' , OC(O)R', $C(O)N(R')_2$, $C(S)N(R')_2$, $OC(O)N(R')_2$, SOR', SO_2R' , $SO_2N(R')_2$, $NR'SO_2R'$, $NR'SO_2N(R')_2$, C(O)C(O)R', or $C(O)CH_2C(O)R'$; and y is 0-5;

 R^2 is selected from halogen, NO_2 , [[CN,]] -SR, -N(R)₂, -(T)_nR, or -(T)_nAr² wherein T is an optionally substituted C_{1-4} alkylidene chain wherein up to two nonadjacent methylene units of T are optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NRCO₂, CO, CO₂, CONR, CSNR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O); n is 0 or 1; Ar² is an optionally substituted aryl group selected from a 5-6 membered monocyclic or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur wherein Ar² is independently optionally substituted with up to five substituents selected from Q-RX; wherein Q is a bond or is a C1-C6 alkylidene chain wherein up to two non-adjacent methylene units of Q are optionally replaced by CO, CO₂, COCO, CONR, CSNR, OCONR, NRNR, NRNRCO, NRCO, NRCS, NRCO2, NRCONR, NRCSNR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; and each occurrence of R^X is independently selected from R', halogen, NO₂, CN, OR', SR', N(R')₂, NR'C(O)R', NR'C(S)R', $NR'C(O)N(R')_2$, $NR'C(S)N(R')_2$, $NR'CO_2R'$, C(O)R', CO_2R' , OC(O)R', C(O)N(R')₂, C(S)N(R')₂, OC(O)N(R')₂, SOR', SO₂R', SO₂N(R')₂, NR'SO₂R', $NR'SO_2N(R')_2$, C(O)C(O)R', or $C(O)CH_2C(O)R'$;

 R^{3} is hydrogen or an optionally substituted $C_{1\text{--}4}$ aliphatic group;

X is selected from a valence bond, O, S, or NR;

 R^4 is selected from -R, -U-Ar³, or -(U)_jCy³; U is an optionally substituted C_{1-6} alkylidene chain wherein up to two non-adjacent methylene units of U are optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NRCO₂, CO, CO₂, CONR, CSNR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O); j is 0 or 1; Ar³ is an optionally substituted aryl group selected from a 3-8 membered monocyclic or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and Cy^3 is an optionally substituted group selected from a 3-7-membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10-membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein Ar^3 and Cy^3 are each independently optionally substituted with up to five substituents selected from Y-R^Z; wherein Y is a bond or is a C_1 - C_6 alkylidene chain wherein up to two non-adjacent

methylene units of Y are optionally replaced by CO, CO₂, COCO, CONR, CSNR, OCONR, NRNR, NRNRCO, NRCO, NRCS, NRCO₂, NRCONR, NRCSNR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; and each occurrence of R^Z is independently selected from R', halogen, NO₂, CN, OR', SR', N(R')₂, NR'C(O)R', NR'C(S)R', NR'C(O)N(R')₂, NR'C(S)N(R')₂, NR'CO₂R', C(O)R', CO₂R', OC(O)R', C(O)N(R')₂, C(S)N(R')₂, OC(O)N(R')₂, SOR', SO₂R', SO₂N(R')₂, NR'SO₂R', NR'SO₂N(R')₂, C(O)C(O)R', or C(O)CH₂C(O)R'; or

wherein R⁴ and R, taken together with the nitrogen form an optionally substituted 5-8 membered heterocyclyl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

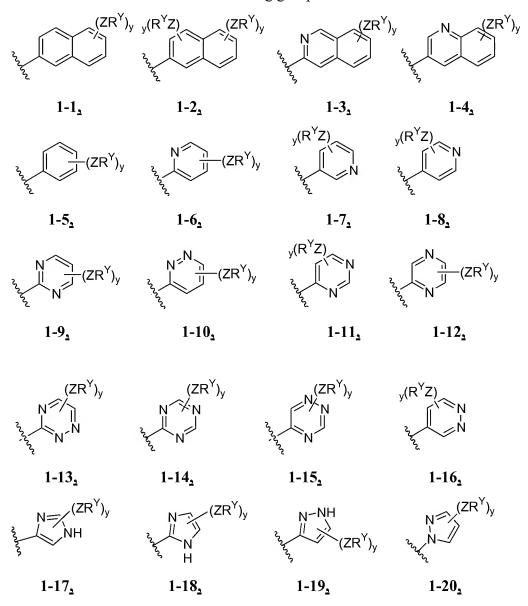
each occurrence of R is independently selected from hydrogen or an optionally substituted C_{1-6} aliphatic group, or two R on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and

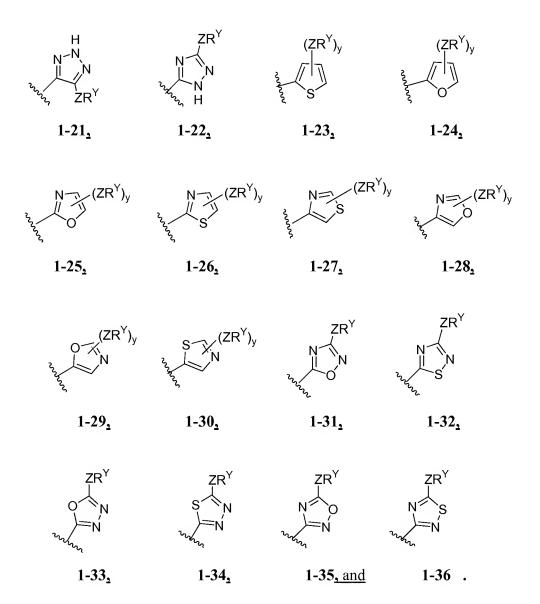
each occurrence of R' is independently selected from hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 3-10 ring atoms, or wherein two R on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur,

provided that:

- a) when X is NR; R, R^3 , and R^4 are each hydrogen; R^2 is - $(T)_nR$ wherein n is 0 and R is hydrogen; and R^1 is - $(L)_mAr^1$ wherein m is 0; then Ar^1 is not:
 - i) 4-Cl or 4-OMe phenyl; or
 - ii) 3-CF₃ phenyl;
- d) when X is a valence bond; R^4 is hydrogen; R^3 is CH_3 ; R^2 is either chloro or hydrogen; and R^1 is $-(L)_mAr^1$ wherein m is 0, then Ar^1 is not 3-trifluoromethyl phenyl or 2-fluoro-5-trifluoromethyl phenyl;
- e) when X is a valence bond; R⁴ is methyl; R³ is hydrogen; and R² is eyano, then R⁴ is not phenyl

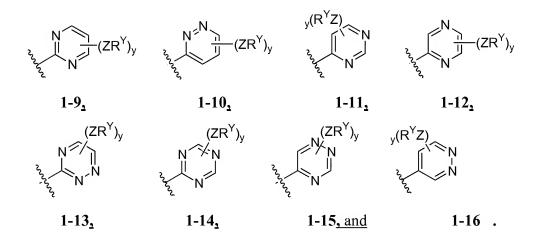
- f) when X is a valence bond; R^4 is methyl; R^2 is -(T)_nR wherein n is 0 and R is hydrogen; R^3 is hydrogen; and R^1 is -(L)_mAr¹ wherein m is 0; then Ar¹ is not 4-tolyl;
- g) 2-[2,4-bis(1,1-dimethylpropyl)phenoxy]-N-[4-[1,6-dihydro-3-methyl-7-(4-nitrophenoxy)-6-oxo-5H-pyrazolo[4,3-c]pyridazin-5-yl]phenyl]-butanamide is excluded.
- 2. (Currently amended) The compound according to claim 1, wherein R^1 is $-(L)_m A r^1$ and $A r^1$ is selected from one of the following groups:



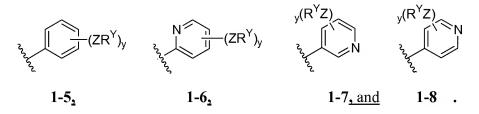


3. (Currently amendeds) The compound according to claim 2, wherein Ar¹ is selected from one of the following groups:

$$(ZR^{Y})_{y}$$
 $(ZR^{Y})_{y}$
 $(ZR^$



4. (Currently amended) The compound according to claim 3, wherein Ar¹ is selected from one of the following groups:



5. (Original) The compound according to claim 2, wherein R^1 is $-(L)_m$ - Ar^1 , m is 1 and compounds have the formula **IA-3**:

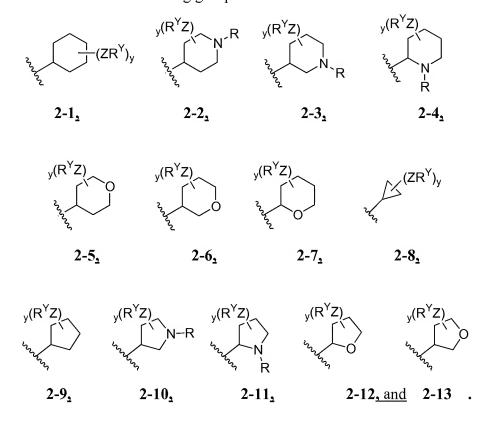
6. (Original) The compound according to claim 2, wherein Ar^1 is phenyl with 0-5 occurrences of ZR^Y and compounds have the formula **IA-1-5**:

IA-1-5

7. (Original) The compound according to claim 1, wherein R^1 is $-(L)_m$ -Cy¹ and compounds have the formula IA-2:

$$\mathbb{R}^3$$
 \mathbb{R}^2
 \mathbb{N}
 \mathbb{N}

8. (Currently amended) The compound according to claim 7, wherein Cy¹ is selected from one of the following groups:



9. (Original) The compound according to claim 2, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NRCO₂, CO, CO₂, CONR, CSNR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O) and m is 1.

- 10. (Original) The compound according to claim 9, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by CO, CO₂, CONR, CSNR, SO₂NR, and m is 1.
- 11. (Original) The compound according to claim 1, wherein R¹ is -(L)_mR, L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NRCO₂, CO, CO₂, CONR, CSNR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O), R is an optionally substituted C₁₋₆ aliphatic group and m is 1.
- 12. (Original) The compound according to claim 1, wherein R^2 is selected from halogen, NO_2 , CN, -SR, $-N(R)_2$, or $-(T)_nR$, wherein R is selected from hydrogen or an optionally substituted C_{1-6} aliphatic group, or two R on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur.
- 13. (Original) The compound according to claim 12, wherein R^2 is selected from -N(R)₂, or -(T)_nR, wherein n is 0, and R is selected from hydrogen or an optionally substituted C₁₋₆ aliphatic group.
- 14. (Original) The compound according to claim 13, wherein R^2 is - $(T)_nR$, wherein n is 0, and R is selected from hydrogen, CH_3 , or CF_3 .
- 15. (Original) The compound according to claim 1, wherein R^2 is $-(T)_nR$, wherein n is 0, R is hydrogen, and compounds have the formula **IB**:

ΙB

- 16. (Original) The compound according to claim 1, wherein R³ is hydrogen, methyl, ethyl, propyl, or isopropyl.
- 17. (Original) The compound according to claim 16, wherein R³ is hydrogen or methyl.
- 18. (Original) The compound according to claim 1, wherein R³ is hydrogen and compounds have the formula **IC**:

$$\begin{array}{ccccc}
H & R^2 \\
N & N & R^1 \\
X & R^4
\end{array}$$

IC

- 19. (Original) The compound according to claim 1, wherein X is selected from a valence bond or NR.
- 20. (Original) The compound according to claim 19, wherein X is NR and R is hydrogen.
- 21. (Original) The compound according to claim 1, wherein X is NR, R is hydrogen, and compounds have the formula **ID**:

ID

22. (Previously presented) The compound according to claim 1, wherein X is O and compounds have the formula **IE**:

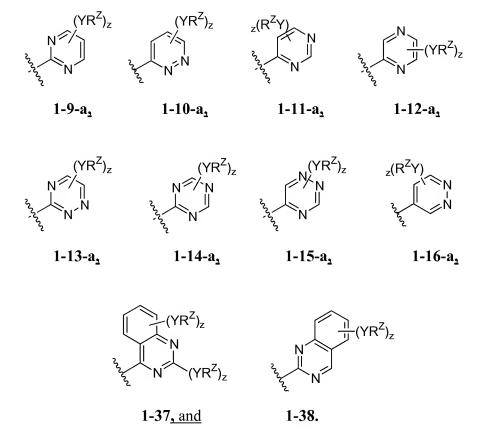
23. (Previously presented) The compound according to claim 1, wherein X is S and compounds have the formula **IF**:

24. (Previously presented) The compound according to claim 1, wherein X is NR, R is hydrogen, R^4 is -U-Ar³ and compounds have the formula **IG**:

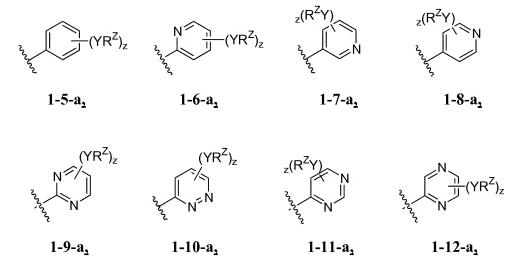
IG

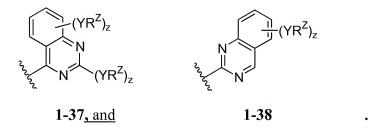
25. (Currently amended) The compound according to claim 1, wherein R⁴ is -U-Ar³ and Ar³ is selected from one of the following groups:

$$z = \frac{z(R^{2}Y)}{|I|} (YR^{Z})_{z}$$
 $z = \frac{z(R^{2}Y)}{|I|} (YR^{Z})_{z}$
 $z = \frac{z(R^{2}Y)}{|I|} (YR^{Z})_{z}$



26. (Currently amended) The compound according to claim 25, wherein Ar³ is selected from one of the following groups:





27. (Currently amended) The compound according to claim 26, wherein Ar³ is selected from one of the following groups:

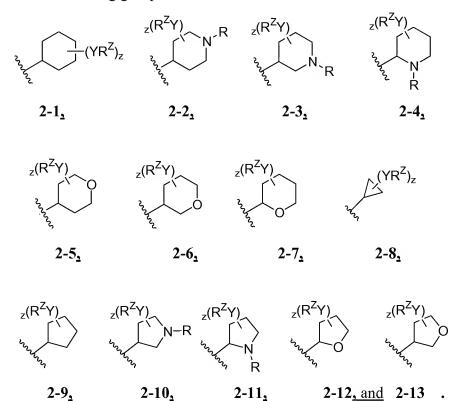
28. (Currently amended) The compound according to claim 1, wherein R⁴ is -U-Ar³ and compounds have one of the following formulas:

$$R_{\lambda}^{3}$$
 R_{λ}^{2}
 R_{λ}^{3}
 R_{λ}^{2}
 R_{λ}^{2}
 R_{λ}^{3}
 R_{λ}^{2}
 R_{λ

29. (Original) The compound according to claim 1, wherein X is NR, R is hydrogen, R^4 is -(U)_jCy³ and compounds have the formula **IG-1**:

IG-1

30. (Currently amended) The compound according to claim 29, wherein Cy³ is selected from one of the following groups:



31. (Original) The compound according to claim 1, wherein X is NR, R and R^4 are hydrogen, and compounds have the formula **IL**:

$$R^3$$
 R^2
 N
 N
 R^3
 R^2
 N
 R^3

IL

32. (Original) The compound according to claim 1, wherein X is a valence bond and compounds have the formula **IM**:

- 33. (Original) The compound according to claim 1, wherein R^4 is R and R is an optionally substituted C_{1-6} aliphatic group.
- 34. (Original) The compound according to claim 1, wherein y is 0-5, and Ar¹ and Cy¹ are independently substituted with 0-5 occurrences of ZR^Y.
- 35. (Original) The compound according to claim 1, wherein y is 0-5, and Ar³ and Cy³ are independently substituted with 0-5 occurrences of YR^Z.
- 36. (Original) The compound according to claim 1, wherein y is 0, and Ar¹ is unsubstituted.
- 37. (Original) The compound according to claim 1, wherein ZR^Y and YR^Z groups are each independently halogen, NO_2 , CN, or an optionally substituted group selected from C_{1-4} aliphatic, aryl, aralkyl, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, -COOR', or $-S(O)_2N(R')_2$.
- 38. (Original) The compound of claim 30, wherein ZR^Y and YR^Z groups are each independently Cl, CF_3 , NO_2 , $-S(O)_2N(R')_2$ or an optionally substituted group selected from $C_{1\cdot4}$ alkoxy, phenyl, phenyloxy, benzyl, or benzyloxy.

39. (Currently amended) The compound according to claim 1, wherein R^1 is $-(L)_m A r^1$, m is 0 or 1, $A r^1$ is phenyl optionally substituted with 0-5 occurrences of $Z R^Y$, and compounds have one of the following formulas **IIA** or **IIA-1**:

40. (Currently amended) The compound according to claim 1, wherein R^2 is $-(T)_nR$, wherein n is 0 and R is hydrogen, R^1 is $-(L)_mAr^1$, wherein m is 0 or 1, Ar^1 is phenyl optionally substituted with 0-3 occurrences of ZR^Y , and compounds have one of the following formulas IIB or IIB-1:

41. (Currently amended) The compound according to claim 1, wherein R^2 is $-(T)_nR$, wherein n is 0 and R is hydrogen, R^3 is hydrogen, R^1 is $-(L)_mAr^1$ wherein m is 0 or 1, Ar^1 is phenyl optionally substituted with 0-5 occurrences of ZR^Y , and compounds have one of the following formulas **HC** or **HC-1**:

42. (Currently amended) The compound according to claim 1, wherein R^3 is hydrogen, R^2 is $-(T)_nR$, wherein n is 0 and R is hydrogen, X is NR, R^1 is $-(L)_mAr^1$

wherein m is 0 or 1, Ar¹ is phenyl optionally substituted with 0-5 occurrences of ZR^Y, and compounds have one of the following formulas **IID** or **IID-1**:

43. (Currently amended) The compound according to claim 1, wherein R^3 is hydrogen, R^2 is -(T)_nR, wherein n is 0 and R is hydrogen, R^1 is -(L)_mAr¹ wherein m is 0 or 1, Ar¹ is phenyl optionally substituted with 0-5 occurrences of ZR^Y , and compounds have one of the following formulas **IIE**, **IIE-1**, **IIF**, **IIF-1**, **IIG**, or **IIG-1**:

44. (Currently amended) The compound according to claim 1, wherein R^3 is hydrogen, R^2 is -(T)_nR, wherein n is 0 and R is hydrogen, X is NH, R^1 is -(L)_mAr¹ wherein m is 0 or 1, Ar¹ is phenyl optionally substituted with 0-5 occurrences of ZR^Y, and compounds have one of the following formulas IIIE, IIIE-1, IIIF, IIIF-1, IIIG, or IIIG-1:

45. (Currently amended) The compound according to claim 1, wherein R^3 and R^4 are hydrogen, wherein R^2 is - $(T)_nR$, wherein n is 0 and R is hydrogen, X is NR, Ar¹ is optionally substituted phenyl, R^1 is - $(L)_mAr^1$, and compounds have one of the following formulas IIH or IIH-1:

$$H_{2}N$$

$$H_{2}N$$

$$H_{2}N$$

$$H_{2}N$$

$$H_{2}N$$

$$H_{2}N$$

$$H_{2}N$$

$$H_{2}N$$

$$H_{3}N$$

$$H_{4}N$$

$$H_{2}N$$

$$H_{2}N$$

$$H_{3}N$$

$$H_{4}N$$

$$H_{5}N$$

$$H$$

46. (Currently amended) The compound according to claim 1, wherein R^3 and R^4 are hydrogen, wherein R^2 is $-(T)_nR$, wherein n is 0 and R is hydrogen, X is a valence bond, Ar^1 is optionally substituted phenyl, R^1 is $-(L)_mAr^1$, and compounds have one of the following formulas IIJ or IIJ-1:

47. (Original) The compound according to any one of claims 39-46, wherein Ar¹ is phenyl optionally substituted with 0-5 occurrences of ZR^Y or wherein Ar¹ is pyridyl optionally substituted with 0-3 occurrences of ZR^Y.

48. (Original) The compound according to claim 47, wherein m is 0 or m is 1 and L is CH_2 ; y is 0-3; and each occurrence of ZR^Y is independently halogen, NO_2 , CN, or an optionally substituted group selected from C_{1-4} aliphatic, aryl, aralkyl, $-N(R')_2$, $-CH_2N(R')_2$, $-CH_2OR'$, -SR', $-CH_2SR'$, -COOR', or $-S(O)_2N(R')_2$.

- 49. (Original) The compound according to claim 48, wherein each occurrence of ZR^Y is independently Cl, CF_3 , NO_2 , $-S(O)_2N(R')_2$ or an optionally substituted group selected from C_{1-4} alkoxy, phenyl, phenyloxy, benzyl, or benzyloxy.
- 50. (Original) The compound according to any one of claims 24-28, wherein Ar³ is phenyl or quinazolyl optionally substituted with 0-5 occurrences of YR^Z or wherein Ar³ is pyridyl or pyrimidinyl optionally substituted with 0-3 occurrences of YR^Z.
- 51. (Previously presented) The compound according to claim 50, wherein U is CH_2 ; X is NH; m is 0 or 1 and L is CH_2 ; y is 0-3; and each occurrence of YR^Z are each independently halogen, NO₂, CN, or an optionally substituted group selected from C_{1-4} alkyl, aryl, aralkyl, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, -COOR', or $-S(O)_2N(R')_2$.
- 52. (Currently amended) The compound according to claim 1, selected from one of the following compounds:

- 53. (Original) A pharmaceutically acceptable composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvent, or vehicle.
- 54. (Original) The composition according to claim 53, additionally comprising an additional therapeutic agent selected from a treatment for Alzheimer's Disease (AD), a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating stroke, an agent for treating cardiovascular disease, an antidepressant, an anti-psychotic agent, or an agent for treating diabetes.
- 55. (Withdrawn) A method of inhibiting GSK-3 kinase activity in a biological sample, comprising the step of contacting said biological sample with:
 - a) a composition according to claim 53; or
 - b) a compound according to claim 1.

- 56. (Withdrawn) A method of inhibiting GSK-3 kinase activity in a patient, comprising the step of administering to said patient:
 - a) a composition according to claim 53; or
 - b) a compound according to claim 1.
- 57. (Withdrawn) A method of treating an autoimmune disease, an inflammatory disease, a metabolic disorder, a psychiatric disorder, diabetes, an angiogenic disorder, tauopothy, a neurological or neurodegenerative disorder, a spinal cord injury, glaucoma, baldness, or a cardiovascular disease, in a patient in need thereof, comprising administering to said patient a composition according to claim 53.
- 58. (Withdrawn) The method according to claim 57, wherein said disease, disorder, or condition is selected from allergy, asthma, diabetes, Alzheimer's disease, Huntington's disease, Parkinson's disease, AIDS-associated dementia, amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease), multiple sclerosis (MS), an injury due to head trauma, schizophrenia, anxiety, bipolar disorder, tauopothy, a spinal cord or peripheral nerve injury, myocardial infarction, cardiomyocyte hypertrophy, glaucoma, attention deficit disorder (ADD), depression, a sleep disorder, reperfusion/ischemia, stroke, an angiogenic disorder, or baldness.
- 59. (Withdrawn) The method according to claim 58, wherein said disease, disorder, or condition is stroke.
- 60. (Withdrawn) The method according to claim 58, wherein said disease, disorder, or condition is Alzheimer's disease.
- 61. (Withdrawn) The method according to claim 57, wherein said disorder is a neurological or neurodegenerative disorder.
- 62. (Withdrawn) A method of decreasing sperm motility in a male patient comprising administering to said patient a composition according to claim 53.

63. (Withdrawn) The method according to claim 57, comprising the additional step of administering to said patient an additional therapeutic agent selected from a treatment for Alzheimer's Disease (AD), a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating stroke, an agent for treating cardiovascular disease, an antidepressant, an anti-psychotic agent, or an agent for treating diabetes, wherein:

said additional therapeutic agent is appropriate for the disease being treated; and said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.